University of Alberta

Visuospatial Perception Disturbances in Alzheimer's Disease

by

J. Michelle Kincade

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

Department of Psychology

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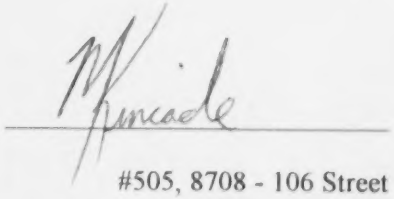

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Edmonton, AB.
T6E 4J5

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University of Alberta

Faculty of Graduate Studies and Research

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled Visuospatial Perception Disturbances in Alzheimer's Disease submitted by J. Michelle Kincade in partial fulfillment of the requirements for the degree of Master of Science.

Dr. Allen Dobbs, PhD

Dr. Alan Kingstone, PhD

Dr. Janet McElhaney, MD

July 17th, 1996
Date

Abstract

Deficits in high level visuospatial abilities in Alzheimer's Disease (AD) patients have been well-documented. The goal of the present study was to determine the degree to which very low level visuospatial abilities are affected in patients with AD. Five experimental tasks were designed to examine performance in three visuospatial categories: visuospatial localization, visuomotor coordination, and motion detection. Sixteen patients diagnosed with probable AD and twenty-six healthy elderly controls participated in this study. The results of the study clearly demonstrate that AD patients are substantially impaired on these low-level visuospatial tasks compared to healthy elderly control subjects. Further analyses suggested the possibility that subgroups of AD patients with differentially affected visuospatial abilities may indeed exist and may warrant further investigation.

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Visuospatial Perception Disturbances in Alzheimer's Disease

Introduction

Alzheimer's Disease (AD) is a neurodegenerative disorder characterized by progressive cognitive impairment in elderly adults. The prevalence of AD in the Canadian population of adults age 65 and over has been estimated to be 8% (Canadian Study of Health and Aging, 1994). In the near future the number of persons with AD will increase as the number of older adults in our population increases exponentially. This has important implications for our health care services and the number of persons utilizing them. As such, it is crucial to gain a better understanding of the disease aetiology, the symptomatology of the disease process and its progression, as well as the practical issues involved in caring for individuals in this population.

While a substantial amount of research has been directed toward identifying the aetiology of AD, a definitive causal factor has eluded researchers. The most widely accepted theory for the development of the disease is a disturbance of the cholinergic system in AD patients (Bartus, Dean, Pontecorvo & Flicker, 1985). Changes in brain levels of cholinergic activity cause disruptions in a variety of cognitive functions, with memory being particularly affected. However, the aetiological basis for this cholinergic disturbance is unknown. A wide variety of hypothetical causes have been put forth, ranging from theories of accumulations of environmental toxins, e.g. aluminum, (Crapper-McLachlan, 1986) to genetic defects involving mutant chromosomal organization (Rapoport, 1990). Perhaps the most promising line of research, put forth recently, suggests a strong association between the accumulation of a protein known as

apolipoprotein E (apoE) and AD (Parer, Davignon, Bouthillier, Kogan, Bertrand & Gauthier, 1993). ApoE protein has been found in high proportions in the neuropathological markers of AD, and has been linked to an E4 allele on chromosome 19. And, it has been demonstrated that people homozygous for the E4/4 allele are at greatest risk for AD. This suggests that there is a relationship between the homozygote E4 expression, the production of apoE protein in the brains of AD patients, and the resultant cognitive and neuropathological changes.

Perhaps the uncertainty in determining the aetiological factors in AD has contributed to the pronounced difficulty in diagnosing AD. Current accepted guidelines set up by the NINCDS-ADRDA Work Group (McKhann, Drachman, Folstein, Katzman, Price & Stadlan, 1984) establish three different levels of diagnostic standards: definite, probable, and possible AD. Definite diagnosis of AD can take place only on histopathological examination obtained at autopsy. There is a pattern of neuropathological markers in certain brain regions that are characteristic of AD. The neuropathology that characterizes AD include: neurofibrillary tangles which are threadlike structures in the cytoplasm; neuritic (or senile) plaques which are essentially large clumps of degenerating neurons that are held together by a protein called amyloid; and massive neural degeneration. In addition to this neuropathology, definitive diagnosis also requires that a clinical determination of probable AD based on cognitive abilities was made antemortem.

Clinically probable AD is largely established by exclusion criteria. That is, in the absence of other neurologic, systemic, or psychiatric causes for dementia, and the absence

of disturbances of consciousness, probable AD can be considered as a diagnosis. The inclusion criteria for diagnosis of probable AD must include the following: dementia established by clinical examination, supported by a dementia screening tool (e.g. Mini-Mental State Examination, Blessed Dementia Rating Scale); and deficits in two or more areas of cognitive function, one of which is progressive memory loss confirmed by neuropsychological examination (McKhann et al., 1984). In addition to memory loss, the other cognitive domains that may be affected in AD include: attention and orientation; language; problem-solving and judgement; executive function; praxis and visuospatial abilities. The majority of research regarding the neuropsychological consequences of AD focuses on changes in memory functions. However, there is potential for a substantial amount of insight to be gained from examination of changes in other aspects of neuropsychological functioning. The purpose of this research project is to provide some information regarding the degree to which visuospatial abilities are affected in AD.

Currently, most clinicians and researchers do recognize that visuoperceptual deficits occur at some point in AD (Lezak, 1995; Zec, 1993). However, these are generally noted to occur in tasks demanding higher level aspects of visual cognition and in patients in later stages of the disease. For instance, it is widely accepted that deficits can be demonstrated on complex neuropsychological tasks that involve constructive abilities, the mental manipulation of spatial information, and visual memory. Some examples of tasks that have been commonly used as measures of visuospatial ability are: Block Design subtest of the WAIS; Mental Rotation of Geometric Figures, and Rey Complex Figure Test (Cronin-Golomb, Corkin, & Growdon, 1995; Cummings & Benson, 1992; Kurylo,

Corkin, Rizzo, & Growdon, 1996,). Although performance on these tests may indeed reflect visuospatial deficits, it is difficult to determine how much of the performance is actually affected by other cognitive functions such as problem-solving, comprehension, executive planning, or motor coordination.

Recently it has also been demonstrated that AD patients can suffer a wide range of deficits on much more basic aspects of vision as well. For instance, a number of researchers have begun to recognize the importance of examining low-level visual functions in AD patients (Cronin-Golomb et al., 1995a; Cronin-Golomb, 1995b; Katz & Rimmer, 1989). Cronin-Golomb (1995b) has documented deficits on a wide range of lower level visual functions that include; stereoacuity, contrast sensitivity, critical flicker fusion, and colour discrimination; and she has reported that deficits can predict performance on several cognitive tasks (1995a). The implication of this new line of research is that visual examinations may have a potential role to play in diagnostic assessments of AD.

The goal of the present study is to determine the degree to which very low level visuospatial skills are affected in AD, if at all. If no differences are noted between healthy elderly controls and AD patients on low level visuospatial tasks, this would suggest that deficits noted in the higher level spatial abilities in AD patients in previous studies are more reflective of cognitive spatial deficits than a lower level perceptual deficit. If AD patients demonstrate deficits on some basic visuospatial abilities (e.g. localizing an object in space), but others are preserved (e.g. making a motor response under visuospatial guidance), this may indicate a dissociation of visuospatial abilities that has ramifications

for the current conception of the visual system (e.g., the "what" and the "where" visual systems; Ungerleider & Mishkin, 1982). A third possibility is that the AD patients will demonstrate substantially impaired performance on all basic spatial skills compared to healthy elderly controls, suggesting that all types of visuospatial abilities are deleteriously affected in AD patients and that no particular types of skills are differentially affected by the disease process. A final possibility is that while all AD patients perform at an impaired level compared to healthy elderly controls on all visuospatial tasks, there may be some individual AD patients who have unusually pronounced difficulties in either all basic spatial tasks, or particular types of spatial tasks, suggesting a gradation of visuospatial deficits in AD patients.

Some researchers have claimed that there are a number of AD patients who seem to suffer from pronounced visuospatial disturbances and have suggested that these patients may represent a unique subtype of AD. These visual deficits have been reported to manifest in a variety of behavioural complaints including: bumping into objects while moving through a familiar environment (Kiyosawa et al., 1989); problems with orientation in familiar and unfamiliar environments (Cogan, 1985); difficulty accurately reaching for objects in their visual field (Mendez, Mendez, Martin, Smyth, & Whitehouse, 1990); deficits in driving abilities (Levine, Lee, & Fisher, 1993); reading problems which they attribute to difficulty following along the lines (not due to language comprehension deficits) (Cogan, 1979); problems in shifting their gaze to an appropriate target; and deficits in recognizing faces (Cronin-Golomb, Corkin, Rizzo, Cohen, Growdon, & Banks, 1991). Furthermore, it has been suggested that for some of these AD patients, these

visual disturbances may be among the earliest and most prominent symptoms to develop. These patients have often received initial consultations from ophthalmologists. It is only after these examinations have failed to reveal any ophthalmologic abnormalities that the patients have then been referred to other medical professionals and subtle cognitive changes revealed. However, in these cases, the cognitive impairment seems to occur secondarily to the visual symptoms. As a result, the development of the disease pathology in these patients may be quite distinct from the "classic" AD pattern of symptoms.

These subjective complaints may appear to have a multitude of possible causes. However, the one factor that is common to each of these complaints and that may help to explain the unusual symptoms is a deficit in visuospatial abilities. Some support for this notion has come from anatomical evidence obtained from functional neuroimaging studies and neuropathological findings.

Kiyosawa and colleagues (1989) assessed eight AD patients of various dementia levels using Positron Emission Tomography (PET). The eight AD patients were divided into two categories: those who reported visuoperceptual complaints (VS) and those that did not (NVS). PET measures brain activity levels by measuring the local cerebral metabolic rates for glucose which is the primary source of energy in the brain. As such, it is an indicator of current activity in certain brain regions. The authors of the study found that the primary visual cortex seemed to have normal activity levels in the VS patients. However, VS patients had significantly decreased activity in both the visual association cortex and the inferior parietal cortex of both hemispheres as compared to controls. Moreover, they localized the area that seemed to be experiencing the majority of the

disturbance in the VS patients to the parieto-occipital junction. This is significant because the posterior parietal region of the brain has been implicated as one of the primary processing areas for visuospatial and visual motion information (Damasio, 1985; Zeki, 1992). The results of this study provide some support for the proposal that extrastriate areas that mediate the visuospatial and motion information may be adversely affected in AD patients that report visual disturbances (VS).

Another line of evidence that supports the possible involvement of specifically visuospatial deficits comes from neuropathological studies. Postmortem examinations of the brains of AD patients are very important because at this point in time, it is only by the identification of specific patterns of neuropathology that a conclusive diagnosis of AD can be made. Hof, Bouras, Constantinidis, & Morrison (1989) conducted a postmortem histopathological examination of the brains of three different groups of subjects: AD patients (AD), AD patients with clinical evidence of Balint's syndrome (ADB), and patients with pure vascular cases of Balint's syndrome (VB). Balint's syndrome is a neurological disorder characterized by a triad of symptoms: " impairment of target pointing under visual guidance (optic ataxia); inability to shift gaze at will toward new visual stimuli (ocular apraxia); and perception and recognition of only parts of the visual field (simultagnosia)". (Hof et al, 1989, p.369) These symptoms bear a remarkable similarity to the previously mentioned behavioural complaints of some AD patients This neurological syndrome is generally thought to occur as a result of bilateral parieto-occipital softenings or infarctions.

Hof et al., (1989) hypothesized that ADB patients would demonstrate a pattern of

pathology unique from that of the typical AD's. The inclusion of the pure vascular Balint's patients served to validate the hypothesis that the parieto-occipital junction was the area responsible for the specific visual deficits described. The results bore out the hypotheses. The brains of the pure vascular Balint's patients were found to have massive bilateral parieto-occipital infarctions. The findings of the ADB pathology in comparison to the AD pathology revealed several important differences. The ADB brains were found to have "less severe pathology in superior frontal gyrus than did the AD cases suggest(ing) that a global caudal displacement in pathology may have occurred such that the *occipital visual areas are far more devastated than usual and the prefrontal association regions exhibit a degree of sparing relative to most AD cases"* (Hof et al, 1989, p. 373). These data suggest that the AD patients who experience prominent visuospatial disturbances may actually do so before the occurrence of any cognitive (e.g. prefrontal) impairments. Furthermore, the authors suggested that these patterns of pathology represent the fact that "the projections to dorsal area 19 (MT or V5) and parietal lobe that are essential for motion detection and visuospatial analysis are devastated" (Hof et al, 1989, p.374).

Thus it is apparent that there are converging sources of evidence that suggest the possibility that a visuospatially affected subtype of AD patients does in fact exist. However, it must be noted that a great deal of the evidence obtained in these studies depends on the reliability of the subjective behavioural reports of the potential AD subtype patients. The aforementioned studies classified the visually symptomatic (Kiyosawa et al., 1989) or Balint's syndrome AD patients (Hof et al., 1989) a priori, based on unclear or subjective evidence. For instance, in the Hof et al. (1989) study, no statements were made

to clarify how a Balint's like syndrome was diagnosed in the AD patients. Similarly, Kiyosawa et al. (1989) classified the AD patients in their study as visually symptomatic or non-visually symptomatic based on subjective behavioural complaints elicited from the patients and their families. Evidence obtained from well-defined and designed psychophysical tasks that could aid in the validation of the reliability of subjective behavioural complaints is missing from these studies. The present study seeks to fill this gap by collecting data from AD patients and age-matched participants on well-controlled visuospatial tasks. The results of this study should provide important insights that may support or refute the existence of an AD subtype with visuospatial deficits.

Objectives

The objectives of this study can be summarized in terms of four major goals: 1) To determine if AD patients differ from healthy elderly controls on carefully selected low level visuospatial tasks; 2) If differences exist between AD patients and normal controls, to determine if these are global spatial deficits (i.e., impaired performance across all spatial tasks), or if deficits are specific to only certain types of spatial tasks while abilities are preserved; 3) To determine if dissociations exist within the AD patient group. That is, to determine if there are either (a) individual AD patients who demonstrate markedly deficient performance on all of the spatial tasks that separates them from the majority of the AD patients, or (b) individual AD patients who demonstrate significantly impaired performance on specific spatial tasks; 4) To determine the extent to which the psychophysical results are related to subjective behavioural complaints elicited from the AD patients.

Task Selection

Visuospatial perception is a broad term that is comprised of many different component abilities. Consequently, there can arise a wide range of visuospatially related deficits. Based on Ogden (1990) and McCarthy & Warrington (1990), the following categories of visuospatial abilities are proposed:

1) Spatial Localization: The ability to accurately perceive the location and orientation of objects in space;

2) Spatial Cognition: The ability to mentally manipulate spatial information;

3) Constructive Ability: The perception of components of a model and the analysis of the spatial relationships between those components as well as the execution of a motor plan designed to duplicate the model;

4) Visuomotor Coordination: The ability to make accurate movements under visual guidance.

5) Visual Motion Detection: The ability to accurately detect and perceive the direction of motion;

6) Visuospatial Attention: The ability to direct visual attention to certain spatial locations.

Several important considerations were taken into account in the selection of the tasks for this study. First, because the goals of this study were to examine very basic visuospatial abilities, the tasks with the lowest level of inherent cognitive demand were chosen. For instance, tasks that involve the manipulation or construction of spatial relations were avoided. Consequently the level of confounds that could be attributed to

higher level cognitive deficits was minimized. The second consideration involved designing tasks that would allow for dissociations to be maximally distinguished if they did, in fact, exist. Finally, an attempt was made to select tasks that closely corresponded with the behavioural complaints reported in the literature by putative visually symptomatic AD patients. Each of the five tasks that were chosen for the present study satisfied the above criteria and fell within three of the above categories: spatial localization, visuomotor coordination, and motion detection.

Spatial Localization and Line Orientation Tasks

The spatial localization perceptual task required the subject to make a two-alternative forced choice decision as to which of two stimulus boxes contained a dot in the same location as it was in a model box. The model appeared at the top of one page and had a small dot placed at a specific point within the box. The two choices appeared at the bottom of the page adjacent to one another and consisted of two equal sized boxes also contained dots. One of the boxes contained a dot that was in exactly the same position as it appeared in the model, the other contained a dot which was slightly displaced from the position in the model. The participant was simply asked to point to the box on the bottom of the page that had the dot in the same position as the one on the top of the page.

In a similar task that involved the perception of line orientation, participants were asked to make decisions about individually presented lines of various orientations. The stimulus in each case was a straight line presented in one of eight possible orientations at the top of the page, simultaneously with two choices at the bottom of the page. The two choices consisted of one rectangular box in the same orientation as the reference line and

one rectangular box that was displaced by 1 clockwise or counterclockwise rotation. The participant was asked to point to the rectangular box that was presented in the same orientation as the stimulus line.

Visuomotor Coordination

In an attempt to determine the degree of visuomotor guidance deficit that these patients may have suffered, the tasks below were matched as closely as possible to the perceptual spatial localization and orientation tasks.

In the Visuomotor Spatial Localization Task, the participants were simply asked to reach out and place the tip of a felt-tip marker directly in the centre of a small circle. The target circle on each trial was in 1 of 8 different spatial locations on the page.

In the Visuomotor Orientation Task, the participant was presented with a reference rectangular box on a piece of paper. Then using an inked stamp of a straight line that was designed to fit within the box, the participants were asked to stamp the orientation of the line inside the center of the rectangular reference box. The box in each trial was 1 of 8 different orientations and the orientations utilized in this task were identical to those that were used in the perceptual line orientation task.

Motion Detection

To investigate the ability to detect motion in AD patients, a variation of the random dot cinematogram display used in two previous studies (Trick & Silverman, 1990; Gilmore et al., 1994) was employed in this test battery. This motion detection paradigm was designed to be a test of both accuracy responses and reaction times at different levels of motion correspondence. Four directions of motion (up/down/left/right) were

represented at 4 different levels of correlated motion. Based on previous research, it was estimated that the motion detection threshold levels of AD patients would range between approximately 10-50% correlated motion (Trick & Silverman, 1990; Gilmore et al., 1994. Therefore, the 4 levels used in this study were: 50%, 35%, 25% and 15%. This design was unique and improved upon previous motion studies in that the response stimulus was presented simultaneously with the actual motion display. The Trick & Silverman study(1991) as well as the Gilmore et al (1994) study required their subjects to make a forced choice decision about the direction of motion after the stimulus display was extinguished. This task, therefore, required a level of working memory ability that is potentially compromised in AD patients and as such was a serious potential confound to the results. The present study, however, required the participant to touch the 1 of 4 possible arrows that corresponded with the direction of motion that they were simultaneously viewing. By designing this task in this manner, possible confounds involving working memory processes are greatly reduced.

Subjective Visuospatial Questionnaire

The literature in this area has suggested that there are some common complaints that are consistently reported by AD patients who are experiencing visuospatial deficits. The questionnaire used in this study was adapted from the Visual Field Disability Questionnaire designed by Mills and Drance (1986) which was originally developed to determine the amount of functional disability that occurred in patients with restricted visual fields. This adapted version was designed to elicit relevant information about the specific types of behaviours and subjective complaints that would be expected to occur in

patients with visuoperceptual deficits.

Methods

Subjects

Sixteen patients diagnosed with probable AD based on NINCDS-ADRDA criteria (McKhann et al., 1984), and their caregivers, participated in this study. The patients in this study were referred to the Memory Disorders Clinic, the Neuropsychology Department or the Seniors Driving Assessment Program of the Northern Alberta Regional Geriatric Program and were all living in the community. The group consisted of 10 females and 6 males with a mean age of 74.81 (sd=5.88) and a mean education level of 10.88 (sd=3.70) years. The AD patient group had a mean Mini-Mental State Examination Score (MMSE) of 25.33 (sd=4.27) out of 30.

Twenty-six healthy elderly volunteers also participated in this study and served as normal control participants. This group was comprised of 13 males and 13 females who were either community volunteers, caregivers or relatives of the AD patients. This control group had a mean age of 73.96 (sd=7.35) and a mean education level of 12.78 (sd=2.90) years. The two groups in this study did not differ significantly either by age, ($t(41)=.39$, ns) or by education level ($t(41)= -1.87$, ns).

An ophthalmologic history was obtained from each individual participant. Participants were excluded from this study if they suffered from glaucoma, macular degeneration, or had cataracts causing visual acuity to be less than 20/70 in the affected eye. In addition, all participants were given a visual screen that included an assessment of visual acuity as well as a peripheral vision assessment.

The visual acuity screen was performed using two separate measures: a Clark's Chart eye exam that consisted of numbers, and a reading test card that consisted of short phrases. Both of these cards were presented approximately 45cm in front of the participant. Because one of the possible visuospatial deficits involves the inability to accurately follow text across a line, the numbers of the Clark's Chart were presented individually. Similarly, only one phrase was presented at a time to the participant on the reading test card. A gross screen of quantative visual perimetry was also performed using a manual perimetry measurement stand (manufactured by C.H. Stoelting Co.) to ensure that no pronounced impairments of the visual fields existed. As a result of this visual screen, it was determined that none of the participants in this study suffered from any significant visual acuity or visual field deficits.

Also, any participant that was noted to have a moderate to severe hand tremor based on clinical observation was excluded from the visuomotor coordination tasks.

Tests and Procedures

Visuoperceptual Questionnaire:

The AD patients and the control participants were asked to answer a number of questions on a questionnaire form. The interviewer questioned each of the participants in regards to their ophthalmologic history and certain behaviours relative to their visual functioning. For the AD patients, corroborative information was also gathered from a caregiver in an independent interview using a similar questionnaire form.

The questionnaire consisted of 31 questions in total. Twenty-eight of the questions asked the participant to rate the frequency of occurrence of a specific

behavioural symptom on a scale that included the following options: Never=0; Rarely=1; Sometimes=2; Frequently=3 and All of the Time=4. The remaining 4 questions required simple yes/no responses. (See Figure 1 in the Appendix for a sample of the questionnaire form.) Of these 31 questions, 21 were questions directly related to visuospatially related complaints, such as: "Do you frequently bump into objects when you are walking through a room?". The other 10 questions served as distractors inquiring about difficulties unrelated to visuospatial deficits, such as: "Do you have trouble seeing differences between colours?". The distractors were included to ensure that a yea-saying bias alone was not responsible for the endorsement of visuospatially-related complaints.

Thus, only the responses on the 21 visuospatially-related complaints were used to comprise the Total Score on the questionnaire. Eighteen of these questions were the based on the rating system and four of the questions were of the yes/no type, thus the total possible score on this questionnaire was 75. In the case of AD patients who also had corroborative reports from caregivers, independent total scores were calculated for the individual reports.

Visuoperceptual Tasks:

Perceptual Spatial Localization Task

This task required the participant to examine a 21.6cm x 27.8 cm (8.5 x 11 inches) stimulus card oriented vertically at a distance of approximately 45cm from the subject. Each card consisted of three black rectangular boxes (9cm x 11cm) on a white background. Each of the boxes contained 1 small black dot (1.0mm in diameter) within the borders of the boxes. One model box appeared on the upper portion of the page in the

centre. The two test choice boxes were side by side on the lower portion of the page. In each of the trials the participant was asked to make a two-alternative, forced choice decision in which they had to choose which of the lower boxes matched the upper box by pointing to the correct box. In each of the model boxes, the dot could appear in 1 of 5 possible locations: centre, upper, lower, right or left portions of the box. For each of these model locations, there were 8 possible trials. For each individual model box, one of the bottom choice boxes matched the model exactly (the dot was in the same position), and the other bottom choice box was a distractor with the dot displaced by one of the following amounts: 6mm, 9mm, 12mm, 15mm in either horizontal direction (for the left and right model positions) or in either vertical direction (for the upper, lower, and centre model positions). Therefore, there were 8 possible stimulus cards for each of the 5 model dot positions for a total of 40 trials. The correct box was randomly and equally distributed between the left and right boxes. (See Figure 2 in the Appendix for a sample of a stimulus card used in this task.) Prior to the administration of the 40 test trials, the participant was presented with 3 practice cards: 1 with a centre dot with the distractor displaced by 1.5mm; 1 with an upper dot with a distractor displaced by 1.2mm and 1 with a right-sided dot with the distractor displaced by 6mm). If the participant failed any of the practice trials, the correct choice was shown to the to ensure comprehension of the task instructions. If the participant failed more than 1 of the practice cards, the same practice set was repeated until the participant identified the correct choice in all 3 cards. If the participant passed each of the practice cards, the test trials were then administered. The instructions for this task were given at a very basic level and repeated as often as required

to ensure adequate comprehension and to minimize cognitive demand and memory load for the task. Scoring Protocol: Each participant received a score of 1 for each correct response and a score of 0 for each incorrect response on each trial. The scores for each trial were summed to give the total correct score out of a possible total score of 40.

Perceptual Line Orientation Task

The stimulus cards in this task presented in the same manner as the dot localization task. The stimulus cards were also 21.6cm x 27.8cm (8.5x11 inches) white sheets. At the centre of the top portion of the page, a straight line (6cm in length, 0.1cm in width) served as the reference line and was presented in 1 of 8 possible orientations; 0, 20, 45, 70, 90, 110, 135,160 degrees. In the bottom left and right quadrants two choice rectangular boxes were presented. The rectangular boxes were 8cm in length and 0.5cm in width. One of the 2 rectangular boxes was in the same orientation as the reference line at the top of the page, while the other box was tilted 1 rotation, either clockwise or counterclockwise, from the model line (See Figure 3 in the Appendix for a sample of a stimulus card.). For instance, if the presented line was at a 45 degree angle, one of the rectangular boxes would also be tilted 45 degrees while the other box could be a distractor tilted at either 20 or 70 degree angle. The participant was asked to choose which of the two boxes was in the same orientation as the reference line at the top of the page. For each of the 8 possible orientations of the reference lines, there were two test condition: one distractor box that is one rotation clockwise or one rotation counterclockwise from the reference line. Therefore, there were 16 possible tests of the 8 different line orientations. Each of the 16 tests were presented twice, for a total of 32 trials. Again the correct choice was randomly

and equally distributed between the left and right sides. The administration of these 32 test trials was preceded by 3 practice trials. If the subject failed any 1 of the 3 practice trials, the error was pointed out to them and explained, and the same 3 practice trials were re-administered until the participant was able to pass all 3. Again, instructions for this task were presented at a very basic level and could be repeated as many times as possible to ensure minimal cognitive demand. Scoring Protocol: Each participant received 1 point for each correct response and the total score was calculated out of a total possible score of 32.

Visuomotor Coordination Tasks

Visuomotor Spatial Localization Task

A clipboard was mounted vertically on a wall approximately 45cm in front of the participant at eye level. The stimulus sheets in this study were white, 21.6cm x 13.9cm (8.5 x 5.5 inches) with the outline of a small black circle (0.5cm in diameter)located in 1 of 8 possible locations (See Figure 4 in the Appendix for a sample stimulus card.). The 8 possible locations of the circle were as follows: one 7cm above and one 7cm below centre; one 5cm to the left and one 5cm to the right of centre, and 4 oblique positions in each of the 4 visual field quadrants (45, 135, 225 and 315 degrees) that were positioned 7cm from the centre of the page. On each trial the participant was asked to simply reach out and touch the point of a felt-tip marker directly inside the target circle on the paper. Each participant was asked to place the tip of the pen on a fixed marked position on the table in front of them before starting each new trial to ensure the same starting point for each trial. The participants were allowed only 1 attempt for each trial. The participants were

instructed not to rest any part of their hands or fingers against the wall or clipboard while making the mark. There were 3 practice trials prior to the test trials. There were 5 trials for each of the 8 circle locations (presented in a random order), for a total of 40 trials. Task instructions could be repeated as many times as were necessary throughout the task.

Scoring Protocol: As this was a task designed specifically for this study, no established scoring protocol existed. In order to assess the accuracy of the responses on each of the trials, a very simple scoring scheme was developed. Each mark made by the participant was assessed according to which of the following categories it fell into:

0= the mark is completely outside of the outline of the circle.
1= the majority of the mark (>50%) is outside of the circle, but some portion of the mark is inside the circle.
2= the majority of the mark (>50%) is inside the circle with some portion of the mark falling outside the circle.
3= the mark is totally inside the circle but is touching the outline of the circle.
4= the mark is completely inside the circle and not touching any portion of the circle outline.

A higher score on this task indicated a superior performance level. The distinction between a score of 1 or 2 was based on a subjective judgement. For this reason, and to ensure that this was a reliable scoring system, an independent person assessed a random subset of 5 patient and 5 control response sets on this task. The independent scorer was blind to whether the response sets were obtained from either a patient or control participant. An inter-rater reliability coefficient was calculated based on the scores assessed by the independent scorer and the primary investigator. The alpha reliability coefficient obtained for this subset of participants was 0.97. Thus, this scoring scheme was considered tp be an efficient and reliable way to score the 40 trials of the response set. In

order to obtain a total score for the entire task, the scores for each of the 40 trials were summed. Each of the 40 trials was scored out of a possible 4 points, for a total possible overall score of 160.

Visuomotor Line Orientation Task

A white sheet of paper (10.8cm x 13.9cm / 4.3 x 5.5 inches) was mounted vertically on a clipboard approximately 45 cm in front of the participant. Each sheet had the outline of one 8 cm by 0.5cm rectangular box on it. (See Figure 5, Appendix I for a sample of the stimulus sheet.) The box was presented in 1 of 8 possible orientations. The 8 orientations that were used were the same as those that were used in the perceptual line orientation task (i.e., 0, 20, 45, 70, 90, 110, 135 &160 degrees). The participant was then given a rubber stamp with a 6cm by 0.1 cm straight line in the centre of the stamp. They were then asked to place the straight line of the stamp inside the centre of the rectangular box. Again, the participants were instructed to touch the paper with the stamp only once. The participant was instructed to press the stamp on an inkpad that was placed in a fixed position on the table in front of them before each trial, thus a starting point was fixed before each trial. There were 5 trials of each of the 8 possible box orientations, presented in random order, for a total of 40 trials. Scoring Protocol: As with the Motor Dot Localization task, this task was also designed specifically for the purposes of this study and thus there was no existing scoring protocol. In order to assess the accuracy of the participant's responses for these trials, each stamped line was assessed in two domains: orientation and location.

The location assessment was made in a manner similar to the motor dot

localization task, except that in this task, a lower location score indicated a superior performance. The location score for each line was assessed according to which of the following categories it fell under:

3= The line is completely outside of the rectangular box.
2= The line is partially outside and partially inside the rectangular box.
1= The line is completely inside the box, but is touching at least part of the outline of the box.
0= The line is completely inside the box and is not touching any part of the outline.

Again in order to determine the inter-rater reliability that could be obtained using this scoring scheme, an independent person assessed a randomly selected subset of 5 patient and 5 control participant's response sets. The reliability coefficient obtained between the primary investigator and this independent scorer was equal to 0.98 for the location measure.

The orientation score for this task was determined simply by assessing the number of degrees (in absolute values) that the orientation of line produced by the participant, differed from the orientation of the rectangular box. This was determined by using a protractor to measure the angle of orientation of the line, and calculating the difference from the orientation of the box. A lower score on this measure indicated a superior performance on this task. Again, orientation scores were assessed by an independent scorer on a randomly selected subset of 5 patient and 5 control participant's response sets. The inter-rater reliability between this scorer and the primary investigator's results was found to be equal to 0.96.

The 2 scores were calculated individually for each of the 40 trials and summed to give a Total Location score & Total Orientation score. These 2 scores were also combined

to give each participant an Overall Total Score on this task. Lower scores on all of these measures indicates a superior level of performance.

Visual Motion Detection Task

A computerized random dot cinematogram was displayed on a 14 inch computer monitor equipped with a Caroll Touch Screen. The stimulus presentation and timing were controlled by a 386DX PC computer. The rectangular display had an area of 12cm by 10cm and consisted of 100 dots evenly dispersed in the centre of the screen (1dot=4 pixels). The central dot display was flanked on each side by a 3.5cm x 1.5 cm arrow. The arrow in the upper portion of the screen pointed upwards; the arrow in the lower portion of the screen pointed downwards; the arrow on the far left portion of the screen pointed towards the left; and the arrow on the far right portion of the screen pointed towards the right. The dots and arrows were presented as white against a black background. The program was rewritten such that the position of the dots changed every 20 msec. For each particular level of correlated motion, a given proportion of dots was displaced in the same direction. The dots that did not comprise the motion signal moved in random directions. Dots that reached the edge of the display were wrapped around to appear on the opposite side of the display. Also, from one screen to the next, the dots that comprised the motion signal were selected at random. This procedure avoids the "streaming" appearance similar to a waterfall. It also discourages a participant from focussing on 1 dot in the display to determine the direction of motion because it is not informative with respect to direction from one screen to the next. Thus, it encourages the participant to engage in a more global detection process of the motion in the display.

The length of presentation of each trial could last up to 5 seconds and the participant viewed the display from a distance of approximately 45cm. There were 4 possible directions of motion in this task (up, down, left & right). There were 4 possible levels of correlated motion (50%, 35%, 25% & 15%). Therefore, there were 16 possible direction/correlated motion level combinations. There were 3 trials for each of the possible combinations of direction and proportion of correlated motion, for a total number of 48 trials. Each of the possible trial types were presented in a randomly selected order.

For each trial the participants were asked to view the display to determine the direction of motion that they perceived in each display. They were instructed to then touch the arrow on the screen that pointed in the same direction that the dots were moving. The touch screen recorded each response that was made within the 5 second time limit. For touches that were not directly on one of the arrows, the screen recorded the touch as a response to the arrow that was located nearest to the touch. The participants were instructed to respond as quickly as possible, but were also informed that the most important factor was to choose the correct direction. Also, the participants were instructed to take their best guess if they were unable to detect the direction of motion. The length of time between trials was determined by the participants individually, as they had to touch any point on the screen to start the next trial. The instructions could be repeated as often as necessary throughout the task.

To ensure comprehension of the task prior to beginning the 48 test trials, a practice session of 8 trials was administered to each participant. The practice session consisted of a random ordering of 2 trials in each direction at a correlated motion level of

75%. This was purposefully set at a very high proportion of correlated motion in order to ensure that the participants could comprehend and accurately perceive what the motion signal actually looked like. The participants had to perform the last 6 of the practice trials correctly in order to proceed to the test trials. If any participant could not correctly perform the last 6 practice trials after 3 attempts of the practice session, the test trials were not administered. Scoring Protocol: The participant's response and time taken on each trial was recorded by the computer. A scoring program was developed that calculated the accuracy of the participant's response. The participant received a score of 1 for each correct response on a trial and a score of 0 for any incorrect or for a nonresponse on a trial. A nonresponse was defined as a failure to make a choice within the 5 second time limit of each trial. The Total Correct Score was obtained by adding the scores over the 48 trials. The total amount of time taken to complete each of the trials was also calculated. Therefore, the total number of correct responses and the total amount of time taken to respond are the two variables that are reported for the motion detection task

Results

The first objective of this study was to determine if the AD patients had visuospatial impairments as compared to the healthy elderly controls. Two broad separate measurements indicated that they did. First, results from the questionnaire revealed that AD patients reported significantly more subjective visuospatial complaints than the elderly controls, $t(42)=2.30$, $p<.03$. Second, a Multivariate Analysis of Variance (MANOVA) was performed on the experimental tasks to determine if indeed the subjective complaints were reflected in the performance on the actual psychophysical measurements of

visuospatial abilities. The result of an omnibus test comparing the two groups on the overall performance measures on the visuospatial tasks validated the reported complaints. The F-test on this MANOVA, $F(2, 40)=32.00$, $p<.001$, indicated that the AD patients as a group performed significantly worse than the elderly controls on the visuospatial tasks. This result clearly demonstrates that AD patients suffer from marked deficits on all of the low level visuospatial experimental tasks as compared to their healthy elderly counterparts in this study.

The second objective of the study was to determine if performance in a particular domain, or domains, within the visuospatial tasks was impaired for the AD patients. MANOVAs were performed for each of the three visuospatial tasks: perceptual, motor and motion detection. Results showed that there were substantial impairments within each domain for the AD vs. control subjects on the perceptual, $F(2,40)=8.08$, $p<.001$, motor, $F(2,40)=27.34$, $p<.001$, and motion detection tasks, $F(2,40)=9.70$, $p<.001$.

Support for this conclusion is shown in Table 1 which displays the mean scores of the two groups on each of the individual dependent measures within the three visuospatial domains. One or more asterisks beside each mean score for the AD patient indicates that the task was performed at significantly poorer levels than controls based on univariate ANOVA F-tests. This table reveals that AD patients were significantly impaired compared to control subjects on all of the visuospatial tasks. The exception is that AD patients were equal to controls on the total time taken to perform the motion detection task, however, they performed this task significantly worse than the controls in terms of accuracy. Thus it appears then that the AD patients showed a performance deficit on all the tasks in the

study spanning three visuospatial domains.

Table 1
Mean Performance Levels on Visuospatial Tasks by Group

VISUOSPATIAL TASKS:	**GROUP**	
Perceptual Tasks	**AD Patients**	**Elderly Controls**
1. Perceptual Dot LocalizationTask Mean Total Score (/ 40)	34.50*** (5.90)	39.04 (0.81)
2. Perceptual Line Orientation Mean Total Score (/ 32)	30.19** (3.06)	31.70 (0.54)
Motor Tasks		
1. Motor Dot Localization Task Mean Total Score (Higher score indicates superior performance)	86.81* (21.06)	101.54 (18.82)
2. Motor Line Orientation Task Mean Location Score (Lower score indicates superior performance)	25.94*** (7.63)	14.58 (7.31)
3. Motor Line Orientation Task Mean Orientation Score (Lower score indicates superior performance)	76.19*** (10.71)	51.08 (6.57)
Motion Detection Task		
1. Motion Detection Task Mean Total Correct Score (/48)	22.06*** (9.79)	33.15 (6.74)
2. Motion Detection Task Mean Total Time (sec.)	139.91 (ns) (41.84)	121.53 (28.70)

*$p<.05$, ** $p<.01$, *** $p<.001$

In an attempt to clarify the main underlying dimensions that were responsible for the performance on the visuospatial tasks, a factor analysis was performed collapsing across AD and control group performance. From the performance on the six visuospatial dependent measures, the principle components analysis extracted two factors that accounted for 54.8% and 23.1 % of the variance, respectively. Thus the cumulative

percentage of variance represented by these two factors was 77.8%. In order to improve the interpretability of these two factors a varimax rotation was applied to the factor structure and Table 2 displays the loadings of the 6 task variables on these two factors.

Table 2

Varimax Rotated Factor Matrix

	FACTOR 1	FACTOR 2
Motion Task: Total Correct	**.74**	-.41
Perceptual Dot Localization	**.92**	-.22
Perceptual Line Orientation	**.93**	-.03
Motor Dot Localization	.13	**-.79**
Motor Line Orientation: orient. score	-.18	**.82**
Motor Line Orientation: locat. score	-.19	**.90**

Examination of the various loadings of the tasks on the two factors reveals that the two perceptual tasks loaded extremely high onto Factor 1 but comparatively low on Factor 2. Conversely, the motor tasks loaded very high on Factor 2, but very low on Factor 1. This pattern seems to indicate that these two factors may be reflective of differential perceptual and motor dimensions that underlie performance on the visuospatial tasks in this study. The performance on the Motion Detection task seems to be more strongly related to the perceptual factor (loading of .74) than for the motor factor (loading of -.41), suggesting, reasonably, that motion detection is at a more general level, a perceptual task. However, the -.41 loading of the motion detection task on the motor dimension is certainly not insignificant and may suggest that performance on this task may be more dependent on an interplay of these two factors, or conversely, that the ability to detect the direction of motion may be best explained by a different underlying dimension altogether. Because of this possibility, the motion detection task in further analyses will

still be considered as a separate visuospatial domain.

In order to determine if the loading of these two factors is the same for AD patients and elderly controls, a MANOVA was performed on the factor scores. The result indicated that the two groups are, in fact, significantly different on both factors, $F(2, 40)=24.69$, $p<.001$, thus confirming the overall difference between groups on visuospatial tasks. Univariate ANOVAs reveal that the groups are significantly different on both of the perceptual and motor factors, Factor 1, $F(2,40)=7.63$, $p<.009$, and Factor 2, $F=(2, 40)25.80$, $p<.001$, respectively, further supporting that both perceptual and motor guided visuospatial abilities are seriously affected by AD.

The third objective of this study was to determine if there were any dissociations within the AD patient group on the visuospatial tasks. It was hypothesized that dissociations could be demonstrated in two ways: a) individual AD patients who might perform at a level that is so deficient on all of the spatial tasks that it distinguishes them from the majority of AD patients, or b) individual AD patients who perform well below the majority of AD patients on specific visuospatial tasks, but at the same level as the majority on others.

In order to investigate the possibility of dissociations within the AD patient group on the visuospatial tasks, a hierarchical cluster analysis was performed. The six dependent measures of the visuospatial tasks were entered as the variables upon which to classify the AD clusters. A dendogram plot revealed three distinct subgroups of AD patients.

An omnibus MANOVA between the three subgroups indicated that they differed significantly, $F(2,13)=18.59$, $p<.001$. To investigate this difference more specifically,

MANOVA's were carried out for the perceptual, motor, and motion domains and the results revealed that the groups differed on the perceptual, $F(2,13)=7.17$, $p<.001$, and the motor, $F(2,13)=7.68$, $p<.001$, tasks, but not on the motion tasks. This failure to find a significant difference on the motion detection tasks is consistent with the results of the factor analysis that revealed only the perceptual and motor tasks as distinct domains.

In order to determine how each subgroup performed on each task, one-way ANOVAs were conducted for each of the tasks. The results are shown in Table 3. Both of the perceptual visuospatial tasks were found to have significantly different levels of performance between the 3 subgroups: Perceptual Dot Localization, $F(2,13)=18.59$, $p<.001$; Perceptual Line Orientation, $F(2,13)=4.42$, $p<.03$. A Newman Keuls post hoc test determined that groups 1 and 2 did not differ, but groups 1and 3 and 2 and 3 did, indicating that performance in group 3 was significantly worse than performance for groups 1 or 2.

Significant differences were also found to exist between the three groups on the Motor Dot Localization Task, $F(2,13)=7.97$, $p<.01$. Post-hoc comparisons on this task revealed that all groups differed significantly from one another with group 1 having the highest score, group 2 having the second highest score, and group 3 again having the lowest score.

The Orientation score of the Motor Line Orientation Task was also found to be significantly different, $F(2,13)=22.29$, $p<.001$. Post-hoc comparisons between clusters revealed significant differences between each group, with group 1 having the highest performance, group 3 the intermediate score, and group 2 the lowest score.

Univariate ANOVAs on the two dependent measures of the motion detection task indicated that the 3 subgroups were not significantly different on these tasks. However, it should be noted that examination of the mean scores of the 3 groups on the Total Correct score, certainly reveals a trend that is similar to the one exhibited by the groups on the perceptual tasks. That is, while they are not statistically significant differences, group 3 performs worse on this measure than either groups 1 or 2.

Table 3
Mean Performance of AD Clusters on Visuospatial Tasks

VISUOSPATIAL TASKS:	**CLUSTERS**		
Perceptual Tasks	**1 (n=6)**	**2 (n=7)**	**3 (n=3)**
1. Perceptual Dot LocalizationTask Mean Total Score (/ 40)	36.17 (2.23)	37.43 (1.40)	24.33 (7.02)
2. Perceptual Line Orientation Mean Total Score (/ 32)	31.50 (1.22)	30.71 (1.98)	26.33 (5.13)
Motor Tasks			
1. Motor Dot Localization Task Mean Total Score (Higher score indicates superior performance)	103.17 (16.14)	83.86 (8.55)	61.00 (24.98)
2. Motor Line Orientation Task Mean Location Score (Lower score indicates superior performance)	20.67 (4.18)	28.29 (8.16)	31.00 (7.21)
3. Motor Line Orientation Task Mean Orientation Score (Lower score indicates superior performance)	67.00 (5.97)	86.43 (5.32)	70.67 (4.51)
Motion Detection Task			
1. Motion Detection Task Mean Total Correct Score (/48)	25.33 (10.27)	24.29 (7.93)	10.33 (3.22)
2. Motion Detection Task Mean Total Time (sec.)	139.60 (35.82)	136.35 (34.77)	148.82 (78.28)

Together, this cluster analysis reveals an intriguing pattern of performance suggesting 3 distinct AD subgroups. Group 1, appears to represent a group of AD patients who are impaired relative to healthy controls, but in comparison with the other AD patients in this study, they demonstrated superior performance across all 3 task domains.

Group 3 represents the opposite end of this spectrum. This group is comprised of AD patients who demonstrated markedly deficient performance on all of the visuospatial tasks. This group is so impaired on the tasks that they almost always performed the worst on the visuospatial tasks.

Group 2, however, was especially interesting because the patients in this group appeared to exhibit a performance dissociation across the task domains. On the perceptual and motion detection tasks, they performed at a level very similar to the high performing group 1 patients. However, on the motor tasks, the patients in Group 2 had significantly poorer performance than Group 1, and were even more deficient than the low performing patients in Group 3. Thus, the patients in Group 2 suggest a subgroup of AD patients who have relatively intact perceptual skills, but whose visuospatially guided motor skills may be seriously compromised.

An obvious interpretation of these results is that these three subgroups must be unique from one another in some other aspect such as age or dementia severity. However, univariate ANOVA's clearly demonstrated that the groups do not differ significantly by age, $F(2,13)= 2.39$, ns, nor by MMSE scores, $F(2,13)=2.86$, ns.

Finally, it is important to recognize that while the unique performance patterns of the 3 groups suggests that dissociations within an AD patient group may exist, the

number of AD patients in this sample, and in the subgroups are moderate in size. Therefore, as compelling as these results may be, they must be interpreted with caution with respect to indicating the existence of specific subtypes of AD patients with unique visuospatial deficits.

Discussion

The majority of previous studies exploring visuospatial deficits in AD patients have employed very high level visuospatial tasks, such as map-reading tasks, mental rotation tests, maze tests, and constructional tasks (Brouwers, Cox, Martin, Chase et al., 1984; Cummings & Benson, 1992; Eslinger & Benton, 1983). As a result, the findings of these studies may have reflected high level cognitive deficits, such as memory or comprehension impairments rather than a specific visuospatial deficit per se. However, the present study has demonstrated clearly that AD patients do experience visuospatial deficits even at very low perceptual levels. And, it should be noted that the results of the present study cannot be attributed to high level cognitive deficits for a number of reasons. First, as discussed earlier, the tasks were designed carefully so as to test low level visuospatial abilities while minimizing any confounding influences of higher cognitive load, a fact reflected in the overall high scores on the tasks (e.g., on the perceptual tasks AD patients performed at about 90% accuracy). Nevertheless, significant effects emerged between AD patients and controls on the tasks. Second, the AD patients in this study suffered from very mild levels of dementia with a mean MMSE score of only 25/30. Thus, the results of this study can be quite confidently attributed to basic visuospatial deficits.

One important issue that was addressed by this study was whether particular

domains of visuospatial abilities are differentially affected by AD. That is, whether AD patients would experience deficits in some aspects of visuospatial functioning but not in others. The results of various analyses clearly revealed that all of the visuospatial abilities investigated in this study were substantially impaired in the AD patients compared to the healthy elderly control subjects.

These findings may have some implications for the involvement of the specific pathways of the visual system. An extensive amount of research effort has been directed toward understanding the visual system over the years and has resulted in a widely accepted model of a dichotomous organization of anatomical and functional pathways within the visual system (Maunsell, 1987; DeYoe & Van Essen, 1988; Ungerleider & Haxby, 1994; Zeki, 1992). Ungerleider and Mishkin (1982) described these as the "what" and "where" pathways and labelled them as the ventral and dorsal visual streams respectively based on their anatomical relations. The ventral stream, or "what" pathway, is believed to process visual information regarding form and colour. The dorsal stream, or "where" visual pathway, is responsible for the processing of visuospatial and visual motion information. Some studies have suggested that the ventral stream may be more deleteriously affected by the AD process based on results that have demonstrated more marked object recognition than visuospatial abilities deficits (Kurylo, Corkin, Rizzo & Growdon, 1996). However, these results may have been confounded by the fact that the tasks chosen to examine both object recognition and visuospatial abilities were neuropsychological tasks with a high degree of inherent cognitive demand involving extensive problem-solving abilities and comprehension abilities (e.g. WAIS - Picture

Arrangement and the Money Standardized Road Map Test). It would be interesting to compare studies that examined low level measures of object-based and space-based visual abilities to determine if object recognition deficits are still found to be more impaired in AD patients than visuospatial deficits. One reason that it may be important to determine if dissociations in these abilities exist, is that differential psychophysical findings may lead to greater understanding of differences in neurochemical or neuroanatomical characteristics of these separate visual pathways. This may lead to the understanding of preferential vulnerabilities that one system possesses and may, in the long run, help to contribute to our understanding of the disease aetiology.

The final implication of the present study is the possible existence of an AD subgroup with visuospatial deficits. Currently, patients with very different clinical presentations are diagnosed under the rather nebulous category of possible or probable AD. Because definitive diagnosis of AD can only take place on autopsy following the completion of neuropathological studies, there has been a widespread acceptance of the premise that all AD patients express the same types of symptoms and that the disease progresses in the same way across all patients. However, there is a growing effort directed toward identifying subgroups or subtypes of AD that present with different patterns of symptoms that may, in fact, have unique aetiologies (Martin, Browers, Lalonde, Cox, Teleska & Fedio, 1986). In the present study, exploration along these lines was intriguing. Based on a cluster analysis, three distinct groups were identified within the AD patient population.

The first group (Group 1) represented a population of AD patients who, although

more impaired than their healthy elderly counterparts, were actually the highest performing patients on all of these visuospatial tasks. The second group of AD patients (Group 2) was particularly interesting. While this group was significantly impaired the visuospatial tasks compared to healthy elderly controls, they demonstrated a dissociation of performance between the different visuospatial domains assessed in this study. Specifically, this group was able to perform the perceptual visuospatial tasks, including motion detection, as well as Group 1 patients. However, with respect to the motor visuospatial tasks, they were substantially inferior to Group 1. This is a curious finding because it may support some of the speculation that has been raised about a functional dissociation within the dorsal visual stream itself.

Recent research by Goodale and Milner (1992) studying a neurological patient with brain damage induced by carbon monoxide poisoning, has demonstrated an apparent dissociation between perceptual and motor visuospatial abilities. Specifically, they have demonstrated that their patient is profoundly impaired on tasks requiring only perceptual visuospatial analysis, however, when she is engaged in a task that requires a motor response under visuospatial guidance, she is remarkably accurate (Goodale, Milner, Jakobson & Carey, 1991). These researchers have interpreted this finding to suggest that the visual system may display functional and possibly anatomical dissociations within the dorsal stream (e.g., "where" and "how" pathways). The potential finding of a visuospatial dissociation in a unique neurological population such as the AD patients in Group 2, is exciting and lends support to the possibility of qualitatively different subdivisions within the dorsal visual stream. What was not found, and what would provide converging

support for this dissociation, is an AD subtype that performed poorly on the perceptual tasks and well on the motor tasks.

Finally, the third group of AD patients (Group 3) may represent yet a different kind of AD subgroup. This group performed at a level inferior to normal controls, however, their deficits were so pronounced on all of the visuospatial tasks that it further distinguished them from the other AD patients. These patients did not demonstrate the dissociation that Group 2 did, that is, performing well on most tests but being severely affected on one. What is remarkable about this group of AD patients, is that they were not significantly different from the other patients in this study by either age or MMSE scores. In fact, none of the three clusters of AD patients were significantly different from one another based on either age or MMSE. As noted earlier, one key point to emerge from this finding is that the different performance levels of the AD subgroups cannot be attributed to different levels of dementia.

In keeping with this last point, it is worth noting that none of the AD subgroups differed significantly on the number of visuospatially related behavioral complaints that they reported on the questionnaire form. While the number of positively endorsed responses on questionnaire was able to distinguish the AD patient group as a whole from the healthy elderly controls, it was not able to distinguish clusters within the AD group. Of course this may be due to a variety of factors (e.g., reluctance to report behavioral symptoms), however, it is interesting, for instance, that Group 2 did not report more pronounced complaints involving motor visuospatial abilities, such as bumping into objects or difficulty reaching for objects in space than would Group 1. Furthermore, the fact that

Group 3 patients did not report more complaints overall is interesting given their actual performance on the visuospatial tasks. Perhaps the reasonable explanation is that the visuospatial tasks in the present study were much more sensitive in assessing performance abilities than the questionnaire.

An alternative explanation is that no true AD visually symptomatic subtype patients were included in this study. For instance, AD patients such as Hof et al.'s (1994) patients with Balint's syndrome, or Kiyosawa et al.'s (1989) visually symptomatic patients, would have been expected to endorse all of the questions on the questionnaire based on their complaints and as such would have been clearly distinguished from other AD patients in the present study on this basis alone. The fact that AD patients with such profound visuospatial deficits were not observed in the present study suggests that this extreme visuospatial AD subgroup, if it exists, is very rare. The patients in Group 3 came closest to representing such a subgroup, and one might speculate that some of these patients may evolve into a profound visuospatial AD subtype.

Overall, the results of the present study suggest that the degree to which visuospatial abilities are affected in AD patients varies greatly from individual to individual although all AD patients show some significant degree of impairment. The degree to which all tasks are affected is likely to be proportional to the amount of involvement of the posterior parietal regions of the brain as this is the region that has been implicated as the primary processing area of the dorsal visual stream (Haxby, Grady, Horowitz, Ungerleider et al., 1991; Robinson, Goldberg & Stanton, 1978). In some patients, this area may be affected as a result of a global degenerative process. These may be the patients, such a the

Group 1 patients in this study, who demonstrate mild disturbances in all visuospatial domains. In other patients, such as Group 2 patients, some aspects of visuospatial abilities may be more deleteriously affected than others and this may reflect a slight alteration of the pathological involvement. Finally, there may be patients who exhibit more profound impairment on all aspects of visuospatial analyses, such as Group 3, and this may be related to early and devastating effects of a degenerative process affecting vulnerable areas.

The fact that all AD patients in the present study demonstrate low level visuospatial deficits has some very important practical ramifications. For instance, the continued ability to drive is a very important issue that could be deleteriously affected in the AD patients, as has been suggested by some previous studies (Drachman, 1988; Kaszniak, Keyl & Albert, 1991). These previous studies have suggested that driving deficits are due to a global deterioration of cognitive function. The present study suggests that at least some deficits might be attributed specifically to visuospatial deficits.

Additionally, recognizing that AD patients may experience visuospatial deficits should influence everyday caregiver management issues. The potential to gain more understanding about the nature of these visuospatial disturbances in AD patients could help to explain a wide variety of behaviors exhibited by demented individuals that may have previously been attributed to other cognitive changes. Wandering behaviour is an excellent example of an ability that has been ascribed in the past to a memory deficit, however, it may be more appropriately recognized as a visuospatially related deficit. Henderson, Mack & Williams (1989) suggested that the tendency for an AD patient to

wander will be largely determined by the severity of their visuospatial deficits. Supportive of this theory is the finding of De Leon, Potegal & Gurland, (1984) which reported that wandering was more strongly related to signs of parietal lobe impairments than of global disease severity measures. Similarly, the recognition that AD patients do experience extensive visuospatial deficits may also result in the causes for a variety of other behavioral problems to be reconsidered.

Consequently, this may lead to the development of more efficient strategies in coping with AD patients. For instance, in the Levine et al (1993) study, they found that the patient in their study was able to continue to read when he used a card that had a space cut out for the individual words which he could then use to follow across the lines. Had this intervention not been made, he would very probably have discontinued any attempts at reading and this would have been assumed to be a result of his cognitive impairments. Similarly, simple types of interventions may also be developed to compensate for the problems of getting lost, and moving through environments more successfully as well as some of the other complaints that have been mentioned. This would be beneficial to patient in that s/he would be able to continue activities that would have been previously abandoned because of an apparent level of dementia severity. It would also be beneficial to the caregivers or staff in care facilities because they would be able to better understand an individual patient's behavior, and hence, would be better equipped to deal with them effectively. Thus reducing some of the problematic or disruptive activity that may be caused by these individuals. These studies, then, offer the potential to provide improved coping strategies for caregivers of these patients, and may

also facilitate the development of efficient functional and practical guidelines for dealing with AD patients.

In summary, it is apparent from this study that a wide range of insights can be obtained from exploring the visuospatial abilities of AD patients. Perhaps an increased focus directed toward understanding unique symptomatology in other areas of neuropsychological functioning may lead to important advancements in our understanding of this disease. It is certainly the case that further investigations of visuospatial deficits in AD hold substantial promise in this regard and valuable insights will continue to be developed from this exciting avenue of research.

REFERENCES

Bartus, R., Dean, R., Pontecorvo, M., & Flicker, C. (1985). The cholinergic hypothesis: A historical overview, current perspectives, and future directions. Annals of the New York Academy of Science, 444, 332-358.

Blanks, J., Torigoe, Y., Hinton, D., & Blanks, R. (1991). Retinal Degeneration in the Macula of Patients with Alzheimer's Disease. Annals of the New York Academy of Science, 640, 44-46.

Brouwers, P., Cox, C., Martin, A., Chase, T., & Fedio, P. (1984). Differential perceptual-spatial impairments in Huntington's and Alzheimer's dementia. Archives of Neurology, 41, 1073-1076.

Canadian Study of Health and Aging, (1994). Canadian Study of Health and Aging: study methods and prevalence of dementia. Canadian Medical Association Journal, 150, 899-913.

Cogan, D. (1979). Visuospatial Dysgnosia. American Journal of Ophthalmology, 88, 361-368.

Cogan, D. (1985). Visual Disturbances With Focal Progressive Dementing Disease. American Journal of Ophthalmology, 100, 68-72.

Coyle, J., Price, D. & DeLong, M. (1983). Alzheimer's Disease: A Disorder of Cortical Cholinergic Innervation. Science, 219, 1184-1189.

Crapper- McLachlan, (1986). Aluminum and Alzheimer's Disease. Neurobiology of Aging, 7, 525-532.

Cronin-Golomb, A. (1995a). Vision in Alzheimer's Disease. The Gerontologist, 35, 370-376.

Cronin-Golomb, A., Corkin, S., & Growdon, J. (1995b). Visual Dysfunction Predicts Cognitive Deficits in Alzheimer's Disease. Optometry and Vision Science, 72, 168-176.

Cronin-Golomb, Corkin, S., Rizzo, J., Cohen, J., Growdon, J. & Banks, K. (1991). Visual Dysfunction in Alzheimer's Disease: Relation to Normal Aging. Annals of Neurology, 29, 41-51.

Cronin-Golomb, A., Rizzo, J., Corkin, S., & Growdon, J. (1991). Visual Function in Alzheimer's Disease and Normal Aging. Annals of the New York Academy of Science, 640, 28-35.

Cummings, J., & Benson, D. (1992). Dementia: A clinical approach. Boston: Butterworth's.

Damasio, A. (1985). Disorders of Complex Visual Processing: Agnosias, Achromatopsia, Balint's Syndrome, and Related Difficulties of Orientation and Construction. In Mesulam, M (Ed.)1985. Principles of Behavioural Neurology. Philadelphia: F.A. Davis Company.

deLeon, M., Potegal, M. & Gurland, B. (1984). Wandering and parietal signs in senile dementia of the Alzheimer's type. Neuropsychobiology, 11, 155-157.

DeYoe, E., & Van Essen, D. (1988). Concurrent processing streams in monkey visual cortex. Trends in Neurosciences, 11, 219-226.

Drachman, D. (1988). Who may drive?/Who may not? Who shall decide? [Editorial]. Annals of Neurology, 24, 787-788.

Eslinger, P., & Benton, A., (1983). Visuoperceptual performances in aging and dementia: Clinical and theoretical implications. Journal of Clinical Neuropsychology, 5, 213-220.

Farah, M. (1990). Visual agnosia. Cambridge, MA: MIT Press.

Gilmore, G., Wenk, H., Naylor, L. & Koss, E. (1994). Motion Perception and Alzheimer's Disease. Journal of Gerontology, 49, 52-57.

Goodale, M., & Milner, A. (1992). Separate visual pathways for perception and action. Trends in Neurosciences, 15, 20-25.

Goodale, M., Milner, A., Jakobson, L., & Carey, D. (1991). A neurological dissociation between perceiving objects and grasping them. Nature, 349, 154-156.

Haxby, J., Grady, C., Horwitz, B., Ungerleider, L., Miskin, M., Carson, R., Herscovitch, P., Schapiro, M., & Rapoport, S. (1991). Dissociation of object and spatial visual processing pathways in human extrastriate cortex. Neurobiology, 88, 1621-1625.

Henderson, V., Mack, W., & Williams, B. (1989). Spatial disorientation in Alzheimer disease. Archives of Neurology, 46, 391-394.

Hof, P., Bouras, C., Constantinidis, J., & Morrison, J. (1989). Balint's syndrome in Alzheimer's Disease: Brain Research, 493, 368-374.

Katz, B., & Rimmer, S. (1989). Ophthalmologic Manifestations of Alzheimer's Disease. Survey of Ophthalmology, 34, 31-43.

Kaszniak, A., Keyl, P., & Albert, M. (1991). Dementia and the older driver. Human Factors, 33, 527-537.

Kiyosawa, M., Bosley, T., Chawluk, J., Jamieson, D., Schatz, N., Savino, P., Sergott, R., Reivich, M., & Alavi, A. (1989). Alzheimer's Disease with Prominent Visual Symptoms - Clinical and Metabolic Evaluation. Ophthalmology, 96, 1077-1085.

Kurylo, D., Corkin, S., Rizzo, J., & Growdon, J. (1996). Greater Relative Impairment of Object Recognition Than of Visuospatial Abilities in Alzheimer's Disease. Neuropsychology, 10, 74-81.

Levine, D., Lee, J., & Fisher, C. (1993). The Visual Variant of Alzheimer's Disease: A clinicopathological case study. Neurology, 43, 305-313.

Lezak, M. (1995). Neuropsychological Assessment (3rd ed.). New York: Oxford University Press.

Martin, A, Brouwers, P., Lalonde, F., Cox, C., Teleska, P. & Fedio, P. (1986). Towards a behavioural typology of Alzheimer's patients. Journal of Clinical and Experimental Neuropsychology, 8, 594-610.

Maunsell, J. (1987). Physiological evidence for two visual subsystems. In L.M. Vaina (Ed.), Matters of intelligence. (pp. 59-87). Dordrecht, The Netherlands: Reidel.

McCarthy, R., & Warrington, E. (1990). Cognitive Neuropsychology: A Clinical Introduction. (pp. 73-97). Toronto: Academic Press, Inc.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. (1984). Clinical Diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology, 34, 939-944.

Mendez, M.F., Mendez, M.A., Martin, R., Smyth, K., & Whitehouse, P. (1990). Complex visual disturbances in Alzheimer's disease. Neurology, 40, 439-443.

Mills, R. & Drance, S. (1986). Esterman Disability Rating in Severe Glaucoma. Ophthalmology, 93, 371-378.

Morrison, J., Hof, P., & Bouras, C. (1991). An anatomic substrate for visual disconnection in Alzheimer's disease. Annals of the New York Academy of Science, 640, 36-43.

Nissen, M., Corkin, S., Buonanno, F., Growdon, J., Wray, S. & Bauer, J. (1985). Spatial Vision in Alzheimer's Disease: General findings and a case report. Archives of Neurology, 42, 667-671.

Ogden, J. (1990). Spatial abilities and deficits in aging and age-related disorders. In F. Boller and J. Grafman (Eds). Handbook of Neuropsychology, Volume 4. New York: Elsevier Science Publishers B.V. (Biomedical Division).

Poirier, J., Davignon, J., Bouthillier, D., Kogan, S., Bertrand, P., & Gauthier, S. (1993). Apoliprotein E polymorphism and Alzheimer's disease. The Lancet, 342, 697-699.

Posner, M. & Cohen, Y. (1984). Components of attention. In Bouma, H & Bowhuis, D. (Eds) Attention and Performance. New Jersey: Lawrence Erlbaum. p. 531-556.

Rapoport, S. (1990). Topography of Alzheimer's disease: Involvement of Association neocortices and connected regions; pathological, metabolic and cognitive correlations; relation to evolution. In S.R. Rapoport, H. Petit, D. Leys, & Y. Christen (Eds.), Imaging, cerebral topography and Alzheimer's disease (pp. 1-17). New York: Springer-Verlag.

Robinson, D., Goldberg, M., & Stanton, G. (1978). Parietal association cortex in the primate: sensory mechanisms and behavioural modulations. Journal of Neurophysiology, 41, 910-932.

Sadun, A., & Bassi, C., (1990). The Visual System in Alzheimer's Disease. In B. Cohen and I. Bodis-Wollner (Eds) pp 331-347. Vision and the brain: The organization of the central visual system, New York, Raven Press.

Sadun, A., Borchert, M., DeVita, E., Hinton, D.& Bassi, C. (1987). Assessment of Visual Impairment in Patients With Alzheimer's Disease. American Journal of Ophthalmology, 104, 113-120.

Sekuler, R. & Owsley, C. (1982). The Spatial Vision of Older Humans. In R. Sekuler, D. Kline, and K. Dismukes (Eds)pp185-202. Aging and Human Visual Function. New York: Alan R. Liss, Inc.

Spear, P. (1993). Minireview: Neural Bases of Visual Deficits During Aging. Vision Research, 33(18), 2589-2609.

Trick, G., & Silverman, S. (1991). Visual Sensitivity to Motion: Age-related changes and deficits in senile dementia of the Alzheimer's type. Neurology, 41, 1437-1440.

Ungerleider, L., & Haxby, J. (1994). 'What' and 'where' in the human brain. Current Opinion in Neurobiology, 4, 157-165.

Ungerleider, L., & Mishkin, M. (1982). Two cortical visual systems. In Ingle, D, Mansfield, R., and Goodale, M. (Eds). The Analysis of Visual Behaviour. MIT Press, Cambridge.

Van Essen, D., & Maunsell, J. (1983). Hierarchical organization and functional streams in the visual cortex. Trends in Neuroscience, 63, 370-377.

Zec., R.F. (1993). Neuropsychological Functioning in Alzheimer's Disease. In R.W. Parks, R.F. Zec, & R.S. Wilson (Eds.), Neuropsychology of Alzheimer's Disease and Other Dementias (pp. 3-80). New York: Oxford University Press.

Zeki, S. (1992). The Visual Image in Mind and Brain. Scientific American, 241, 150-162.

APPENDIX

Figure 1. Visuoperceptual Questionnaire Form

I would like to ask you a few questions about some things related to your vision. Some of these questions relate very closely to vision, and some may seem like they have nothing to do with vision. However, they are all important to this area of research. It may be difficult to answer some of these questions, but we would just like you to do the best you can. If you feel you are truly unable to make a judgement about some of the questions, then it is alright to answer "Don't know". However, we would appreciate it if you could try to answer all of the questions possible to the best of your ability.

A. Have you ever noticed any of the following:

Never=0 Rarely=1 Sometimes=2 Frequently=3 All of the time=4
Don't Know=99 Not Applicable=88

1. ____ General problems with your vision:
2. ____ Trouble focussing on objects:
3. ____ Tripping over things or bumping into things:
4. ____ Trouble finding objects (ie// in a room, or in a cupboard):
5. ____ Difficulty following along a line of print or finding the next line while reading:
6. ____ Difficulty seeing moving objects accurately:
7. ____ More trouble seeing on cloudy days compared to sunny days:
8. ____ Having objects suddenly appear when you should have noticed them earlier:
9. ____ Trouble finding your own clothing in closets or on a coat rack:
10. ____ Perceiving the richness of colors from time to time:
11. ____ Misreaching for objects or knocking things over when reaching for something:
12. ____ Trouble getting dressed (ie// misaligning buttons, putting clothes on inside out):
13. ____ Getting lost in familiar environments (ie// in own home or neighborhood):
14. ____ Getting lost in unfamiliar environments:
15. ____ Wandering around without a purpose:
16. ____ While driving, trouble interpreting intersections:
17. ____ Difficulty accurately judging distances while driving:
18. ____ Distinguishing one color from another:
19. ____ Difficulty identifying objects in front of you:
20. ____ Difficulty performing simple addition or subtraction equations:
21. ____ Tendency to spill when pouring liquids from one container to another:
22. ____ Changes in your ability to write neatly or coherently:
23. ____ Trouble using keys (ie// trouble fitting a key into a lock):
24. ____ Seeming to have blurry vision
25. ____ Trouble seeing words on the far side of a page, or food on the side of a plate.

Figure 1. Visuoperceptual Questionnaire Form (cont'd)

B. Do you need corrective lenses:
___ all of the time
___ for reading
___ for driving
___ does not need corrective lenses

C. If you wears corrective lenses, does wearing them seem to improve any of the above problems?
YES **NO**

i) If yes, which ones?

D. In the last 3 years, have you been referred to or been seen by an ophthalmologist?
YES **NO**

E. Have you had trouble with everyday activities because of your vision?
YES **NO**

F. Have you had to give up any activities because of your vision?
YES **NO**

Figure 2. Perceptual Dot Localization Task (not actual size)

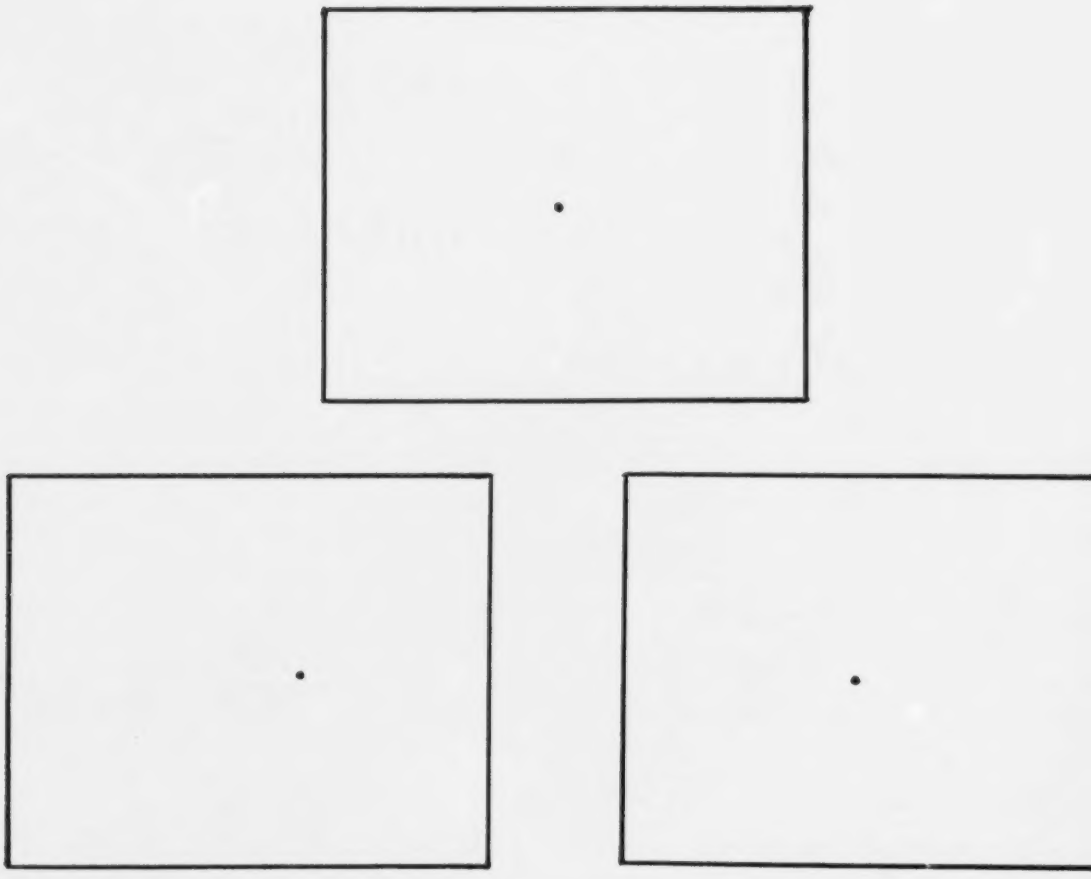

Figure 3. Perceptual Line Orientation Task (not actual size)

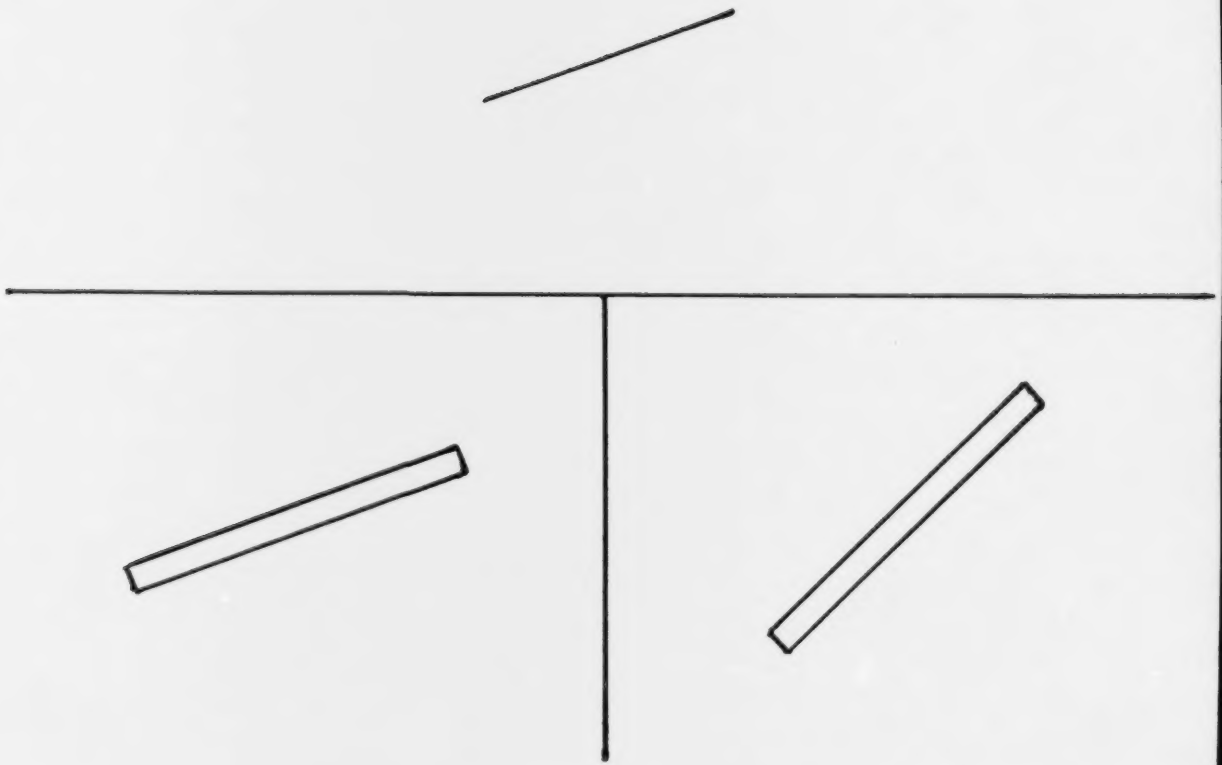

Figure 4. Visuomotor Dot Localization Task

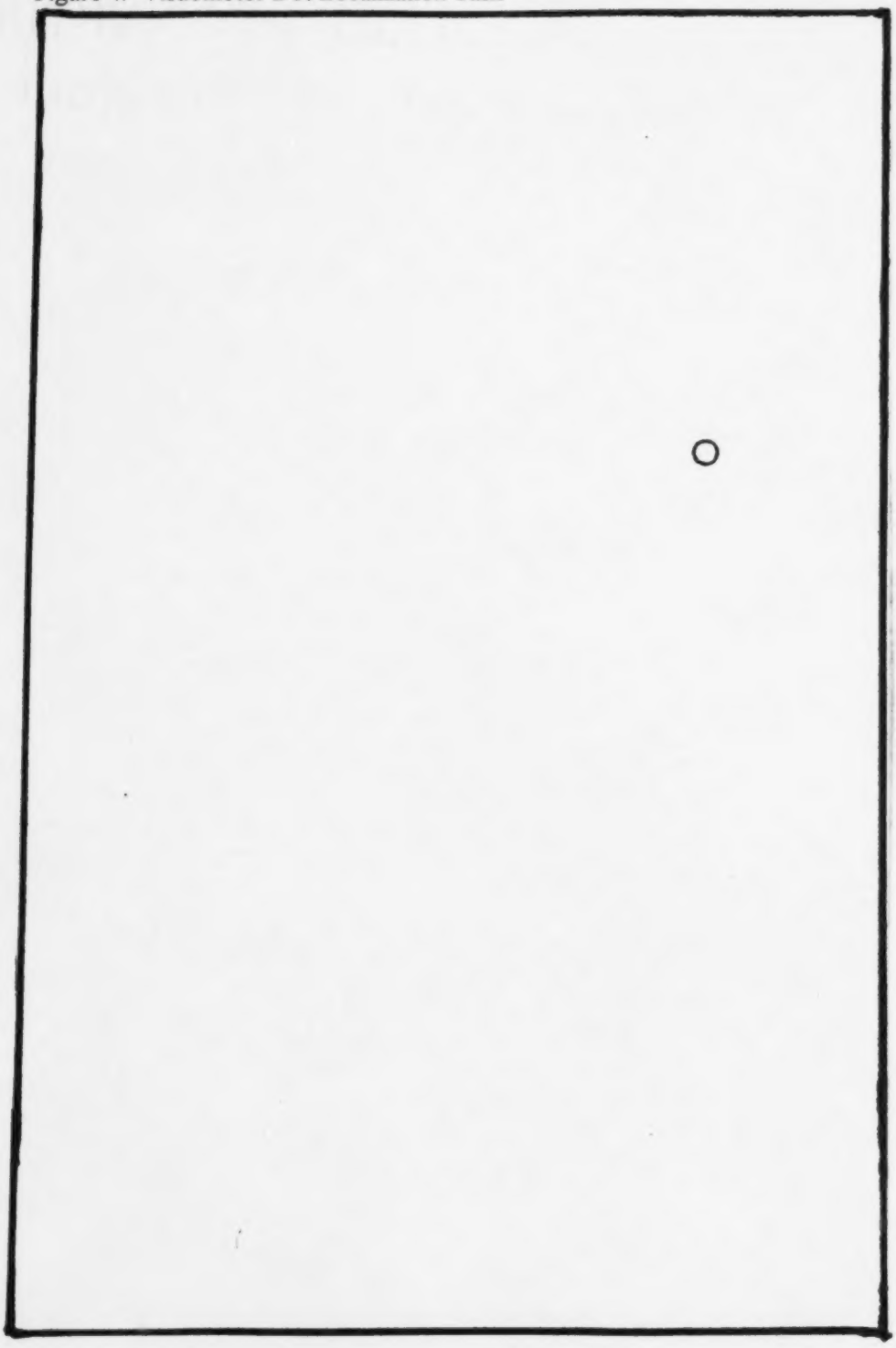

Figure 5. Visuomotor Line Orientation Task